and can recover to its original shape when compression ratio is less than 80% which will be very attractive for bone tissue engineering. SEM analysis shows that the pores in the hydrogel was uniformly present and highly interconnected which is very important for nutrients transplantation. XRD image indicates that both polmers and clay were well distributed. Adding macromolecular crosslinker (PEGDA) into the system can not only increase the biocompatibility but also improve the bone formation compared with the nanocomposite hydrogel without PEGDA.

Discussion and Conclusion: A novel nanocomposite hydrogels composed of exfoliated clay showed attractive fracture strain up to 5000% and good compression strength. This kind of hydrogel was synthesized by in situ photo-polymerization of monomer in the presence of clay, acrylic acid derivatives and macromolecular crosslinker (PEGDA). More attractive part is that the obtained nanocomposite hydrogel has good biocompatibility and can accelerate bone formation. So that we will explore why this kind of hydrogel can accelerate bone formation and find out the best PEGDA molecular weight, clay content and solid content for bone formation.

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Session: Others

292
MODULATION OF SUPERFICIAL ZONE PROTEIN/LUBRICIN/PRG4 BY KARTOGENIN AND TRANSFORMING GROWTH FACTOR-β1 IN SURFACE ZONE CHONDROCYTES IN BOVINE ARTICULAR CARTILAGE

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Introduction: Articular cartilage is an anisotropic structure with a zonal design and consists of surface or superficial, middle, and deep zones. Superficial zone protein (SZP)/lubricin/PRG4 functions as a boundary lubricant in articular cartilage to decrease friction and wear. (Reference 1, 2) As articular cartilage lubrication is critical for normal joint function, the accumulation of SZP at the surface of cartilage is important for joint homeostasis. Recently, a heterocyclic compound called kartogenin (KGN) was found to induce chondrogenic differentiation and enhance mRNA expression of lubricin. (Reference. 3) The objective of this study was to determine whether KGN can stimulate synthesis of SZP in superficial zone articular chondrocytes and synoviocytes.

Subjects and Methods: We investigated the effects of KGN and transforming growth factor-β1 (TGF-β1) on articular cartilage and synovium of the bovine knee joint by evaluating SZP secretion by enzyme-linked immunosorbent assay analysis. Monolayer, micromass, and explant cultures of articular cartilage, and monolayer culture of synoviocytes, were treated with KGN and TGF-β1. Explant was also treated with KGN and IL-1β to evaluate the anti-catabolic effect of KGN. SZP accumulation in the medium was evaluated and mRNA expression was measured through quantitative polymerase chain reaction.

Results: TGF-β1 stimulated SZP secretion by superficial zone chondrocytes in monolayer, explant, and micromass cultures as expected. In addition, SZP secretion was inhibited by IL-1β in explant cultures, and enhanced by TGF-β1 in synoviocyte monolayer cultures. Although KGN elicited a 1.2-fold increase in SZP mRNA expression in combination with TGF-β1, KGN neither stimulated any significant increases in SZP synthesis nor prevented catabolic decreases in SZP production from IL-1β.

Discussion and Conclusion: These data suggest that the chondrogenic effects of KGN depend on cellular phenotype and differentiation status, as KGN did not alter SZP synthesis in differentiated, superficial zone articular chondrocytes. However, these apparent differences between progenitor and differentiated cell types in response to KGN merit additional investigation since important new, mechanistic insights into the effects of KGN may be revealed.

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Session: Disease & Treatment — Tumors

294
DIFFERENTIATION THERAPY OF THE NEOPLASTIC STROMAL CELLS IN GIANT CELL TUMOR OF BONE USING THE U.S. FOOD AND DRUG ADMINISTRATION (FDA)-APPROVED DRUGS, RAPAMYCIN AND SIMVASTATIN

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Background: Giant cell tumor of bone (GCT) is a common neoplasm in Chinese patients, constituting 20% of all benign bone tumors. The stromal cells of GCT are widely accepted to be the primary neoplastic cells, and originate from mesenchymal stem cells (MSC). Since GCT stromal cells could be induced to be mature osteoblasts, our research team has proposed the differentiation therapy of GCT stromal cells. It is noteworthy that rapamycin and simvastatin have been shown to induce osteogenic differentiation in a number of tumor types, and they are FDA-approved drugs and have been safely used in patients for decades. Therefore, we reasoned that they may be developed as adjuvant therapy agents for GCT.

Subjects and Methods: We investigated the effects of rapamycin and simvastatin on cell viability, proliferation and osteoblastic differentiation in GCT stromal cells in vitro. Cell viability was assessed using MTT assay, whereas, cell proliferation by BrdU assay. The markers for assessing the re-differentiation of GCT stromal cells are ALP, RUNX2, and OCN, and the mRNA level of those markers were detected by real-time PCR.

Results: Rapamycin decreased the cell viability and proliferation of GCT stromal cells significantly at 0.05 μM but no further inhibition was observed when increasing the dose of the drug up to 5 μM. Whereas, simvastatin showed a dose-dependent inhibition on cell viability and proliferation in GCT stromal cells. Moreover, the important osteoblastic markers RUNX2 and osteocalcin were up-regulated by both drugs.

Discussion and Conclusion: Rapamycin and simvastatin inhibited cell viability, and proliferation of GCT stromal cells. They also stimulated RUNX2 and osteocalcin gene expression, and may induce differentiation of the tumor cells. Previous studies have shown that simvastatin induces osteoblast differentiation by monitoring Smad signaling and Ras/Rho-mitogen-activated protein kinase pathway (Yamashita et al. 2008), whereas, rapamycin stimulates the osteoblastic differentiation of human embryonic stem cells by blocking the mammalian target of rapamycin (mTOR) pathway and activating the BMP/Smad pathway (Lee et al. 2010). The possibility of using rapamycin and simvastatin to promote the differentiation of GCT stromal cells into mature osteoblasts is appealing. Such a strategy has the dual advantage of preventing further bone destruction as a result of the osteolytic tumor while simultaneously promoting bone formation as the neoplastic cells are differentiated into mature osteoblasts. The mature osteoblasts will eventually undergo apoptosis. It will stop the tumor growth and thus reduce bone resorption.
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Session: Disease & Treatment — Tumors

296
EXPRESSION OF GLYPICAN-3 AND PERIOSTIN IN MUSCULOSKELETAL TUMOR PATIENTS

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Background: Glypican-3 (GPC-3) is an extracellular matrix that functions in cell adhesion, migration and invasion during cell proliferation. It can induce abnormal cells to apoptosis. Additionally, periostin (POSTN) is also extracellular matrix that involve in tissue development and regeneration. This gene can bind to integrin for supporting adhesion and migration of epithelial cells. However, GPC-3 and POSTN expressions in soft tissue sarcoma remain unclear. The purpose of this study was to examine expression of GPC3 and POSTN in neoplastic and non-neoplastic adjacent tissues of musculoskeletal tumor patients.

Subjects and Methods: This research was conducted a cross-sectional study. Twenty musculoskeletal tumor patients who had liposacroma, osteosarcoma, lipoma, giant cell tumor and chondroma were enrolled in this study. The GPC-3